

FIG. IA

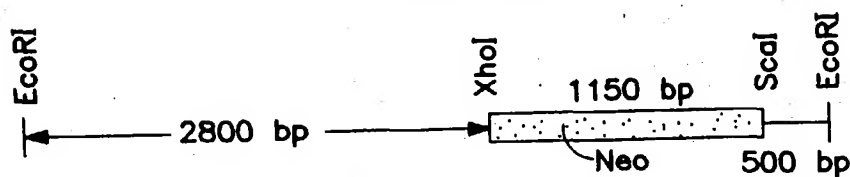


FIG. IB

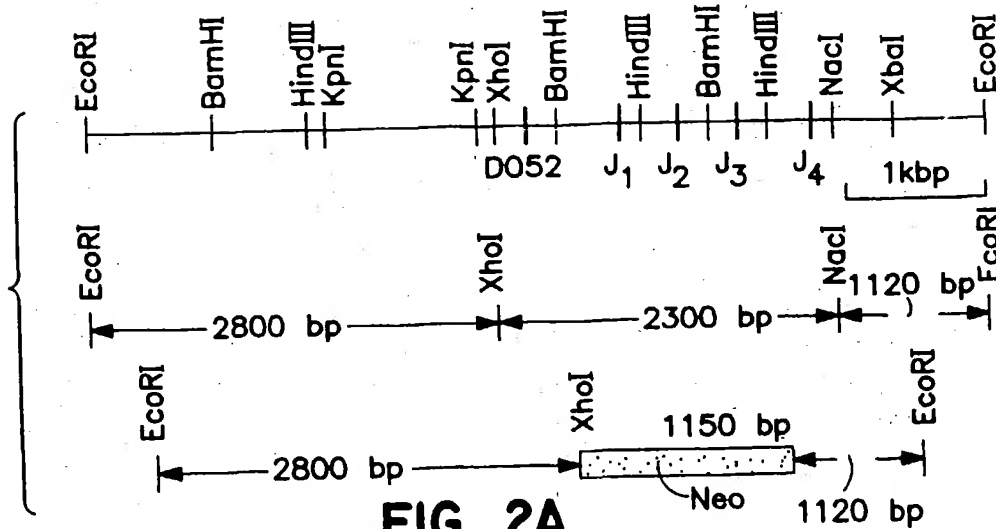


FIG. 2A

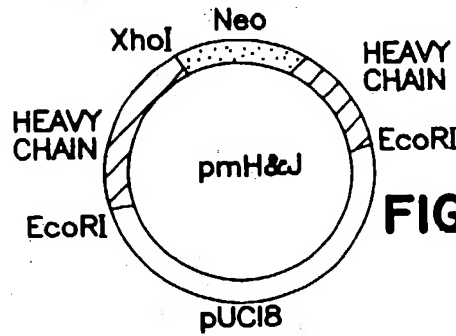


FIG. 2B

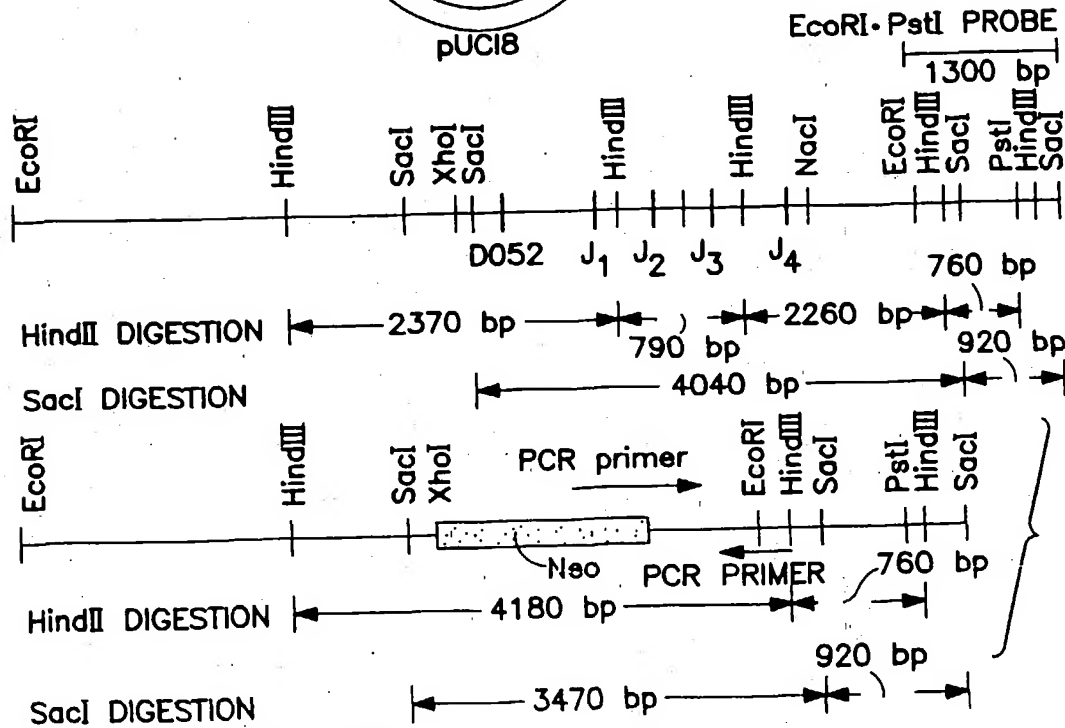
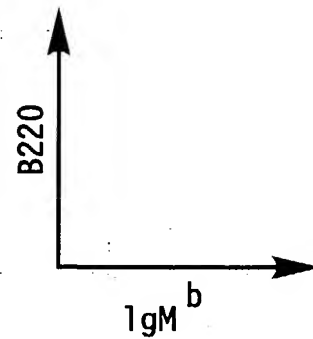
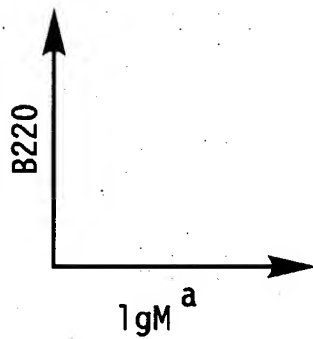
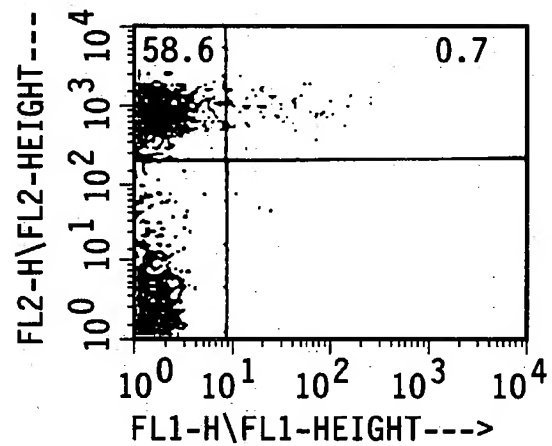
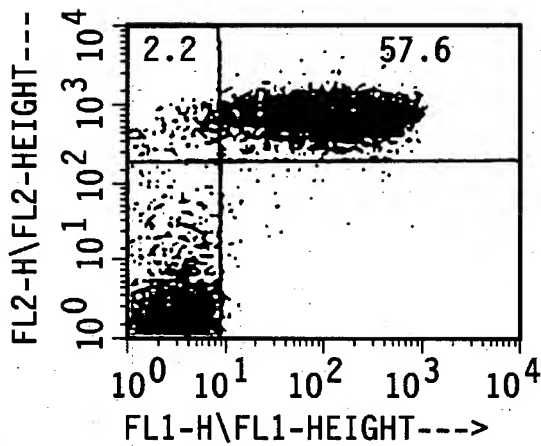


FIG. 2C



a allotype



b allotype

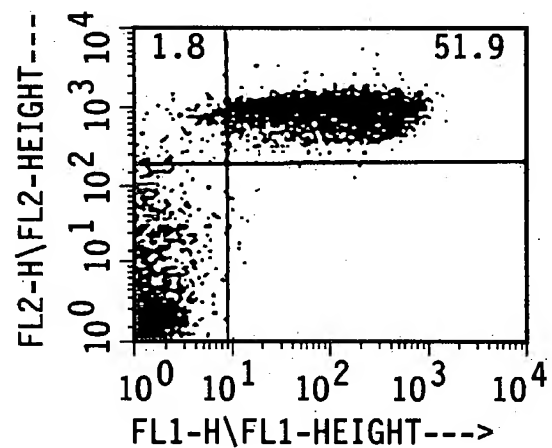
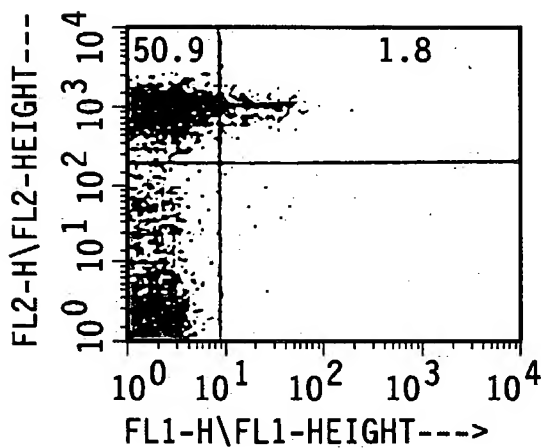
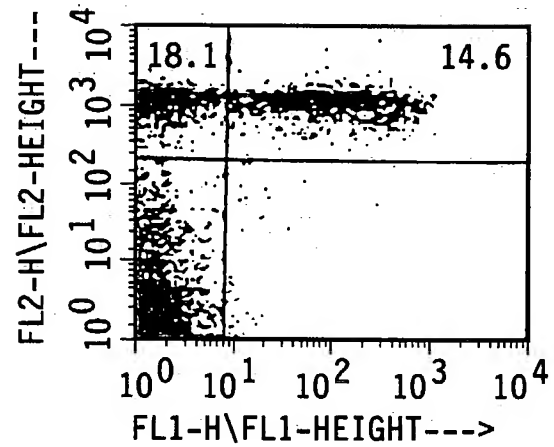
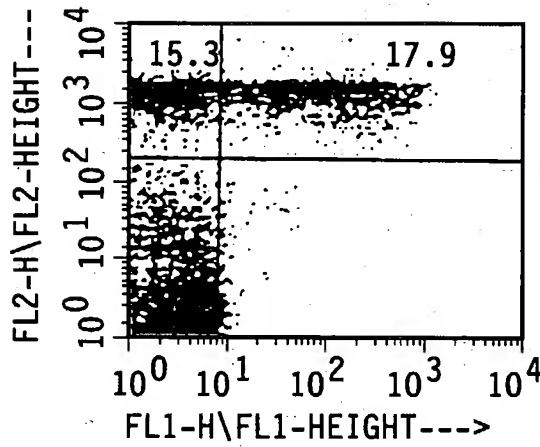


FIG. 3-1

a/bF1



ΔJ_H /bF1

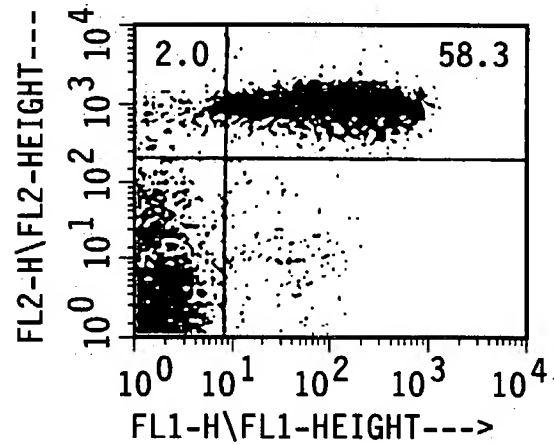
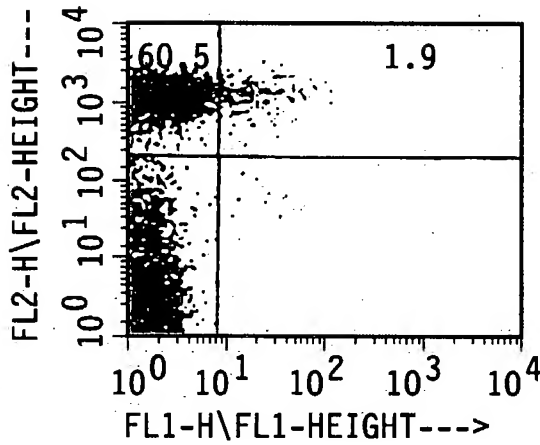


FIG. 3-2

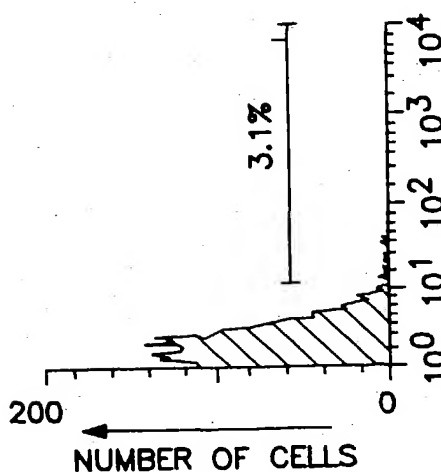


FIG. 4C

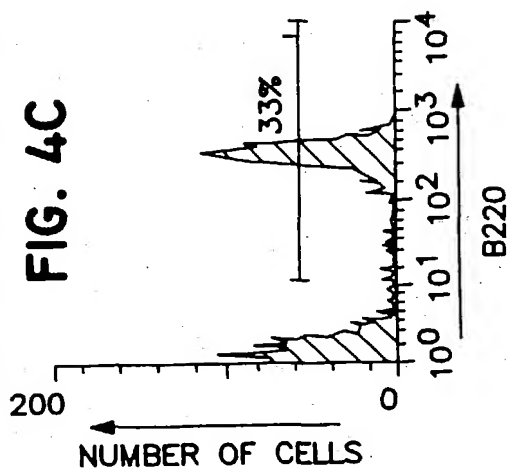


FIG. 4F

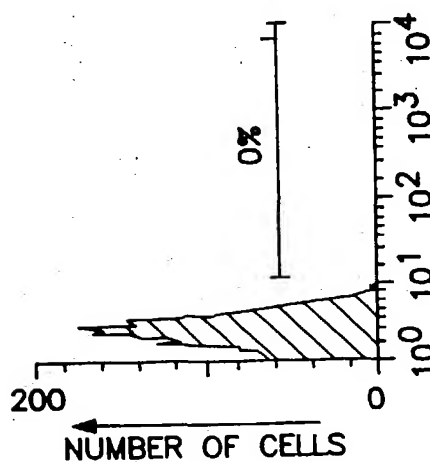


FIG. 4B

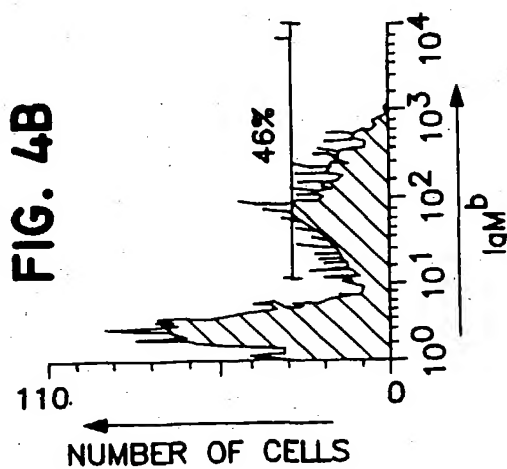


FIG. 4E

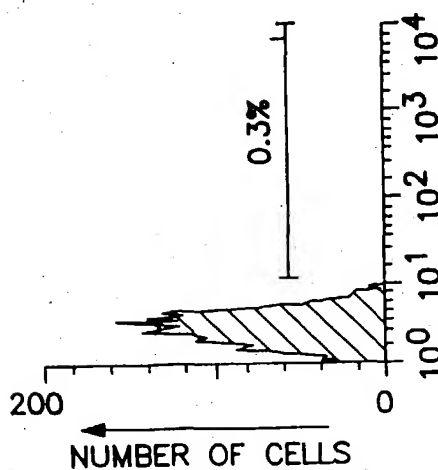


FIG. 4A

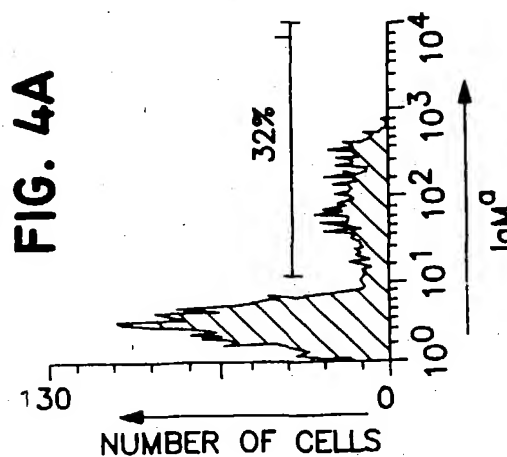


FIG. 4D

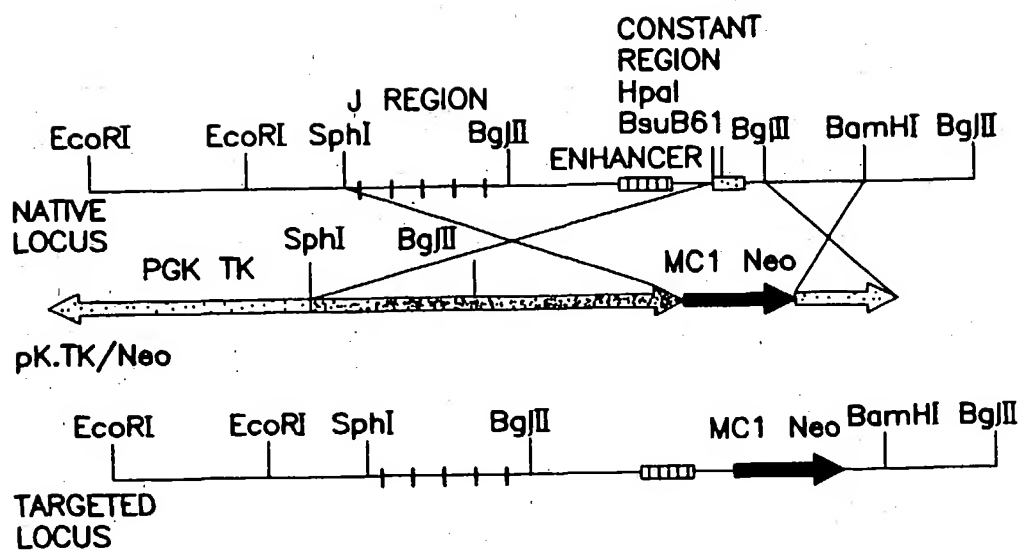


FIG. 5

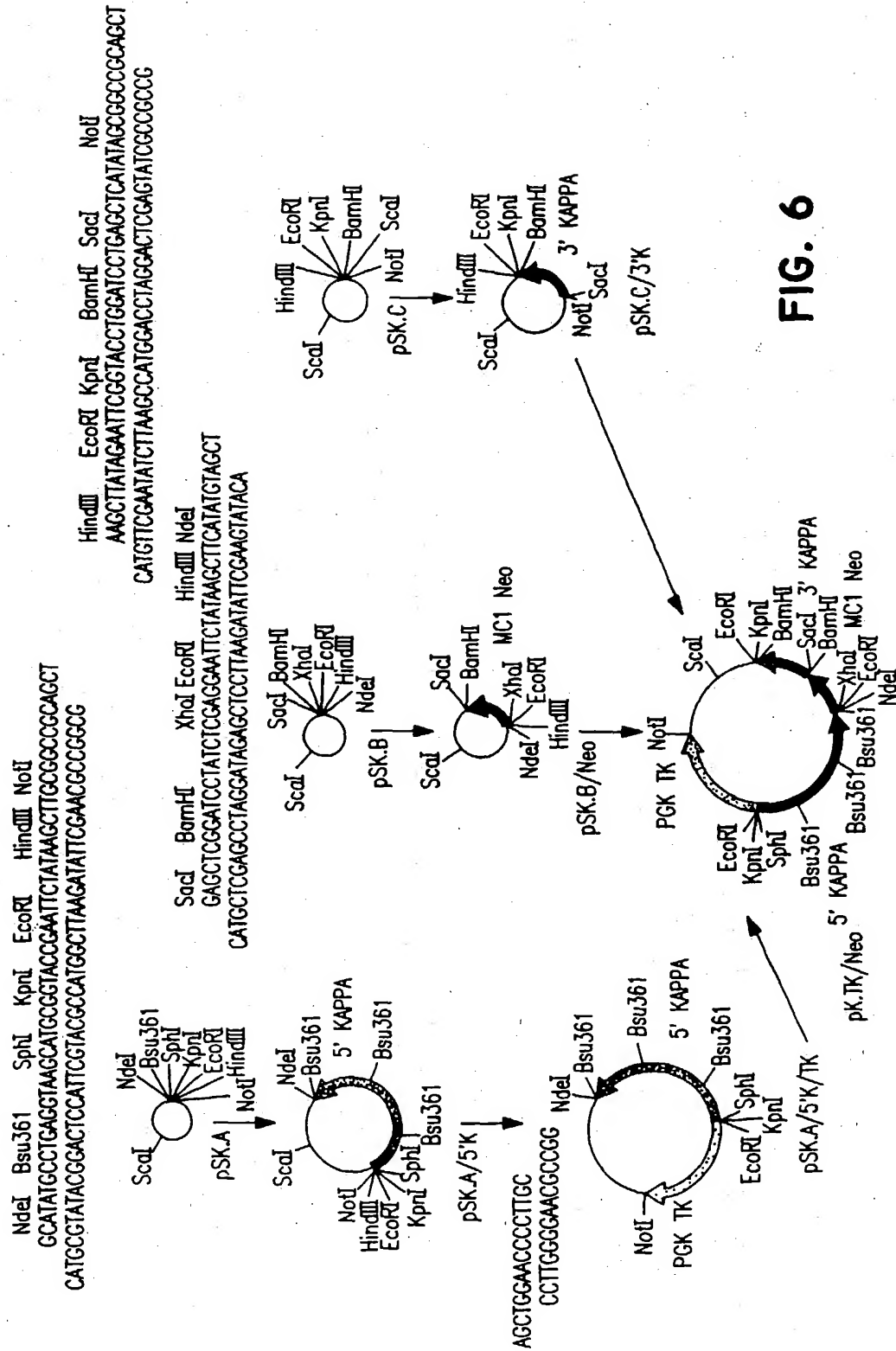


FIG. 6

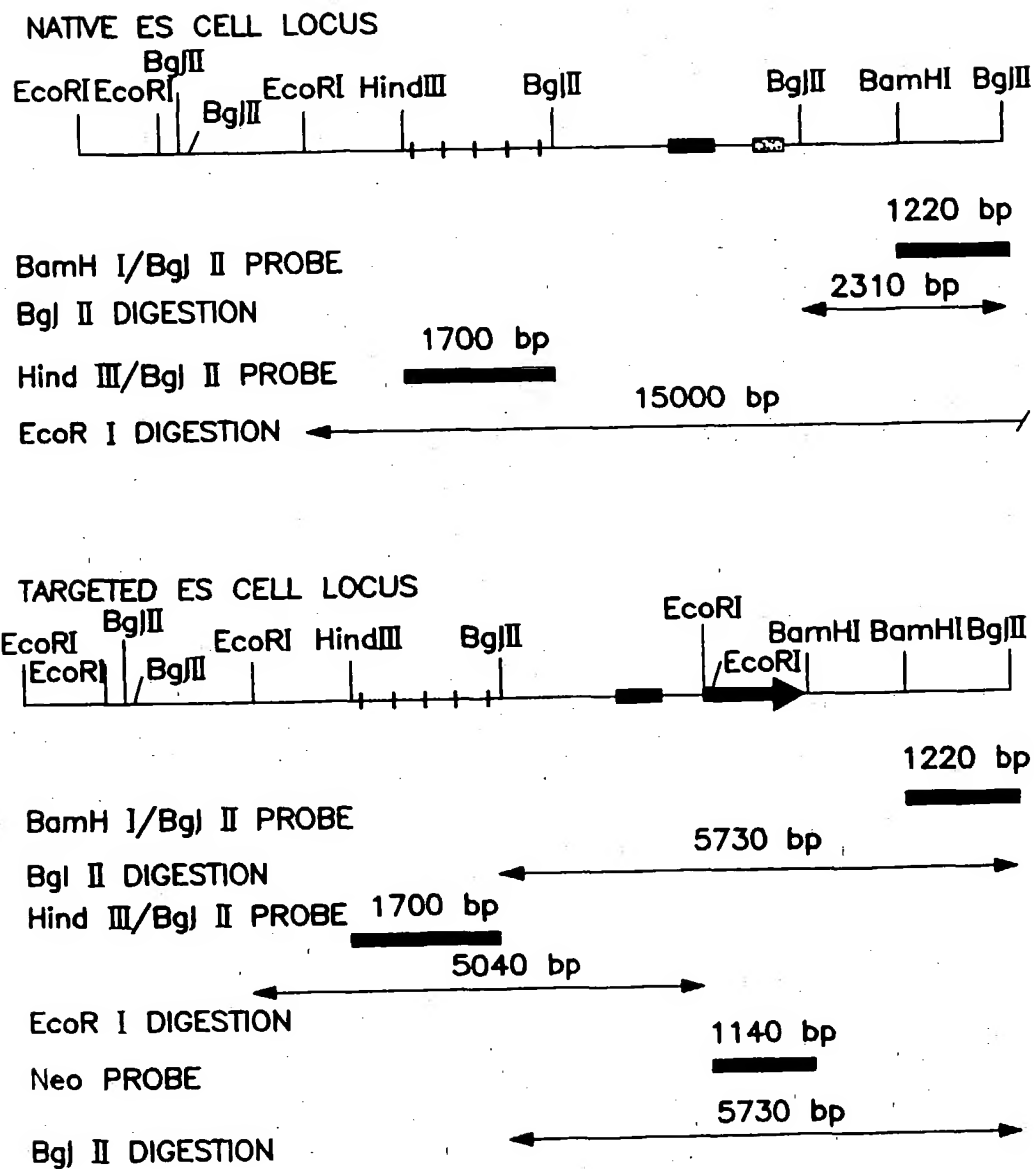
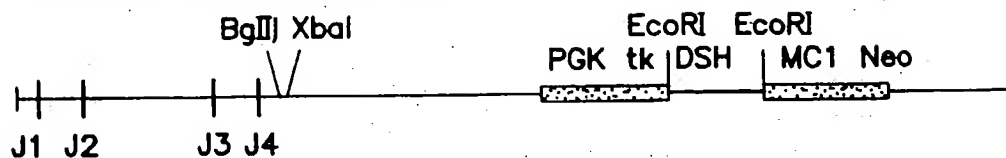


FIG. 7

J REGION KNOCKOUT VECTOR



TARGETING SCHEME

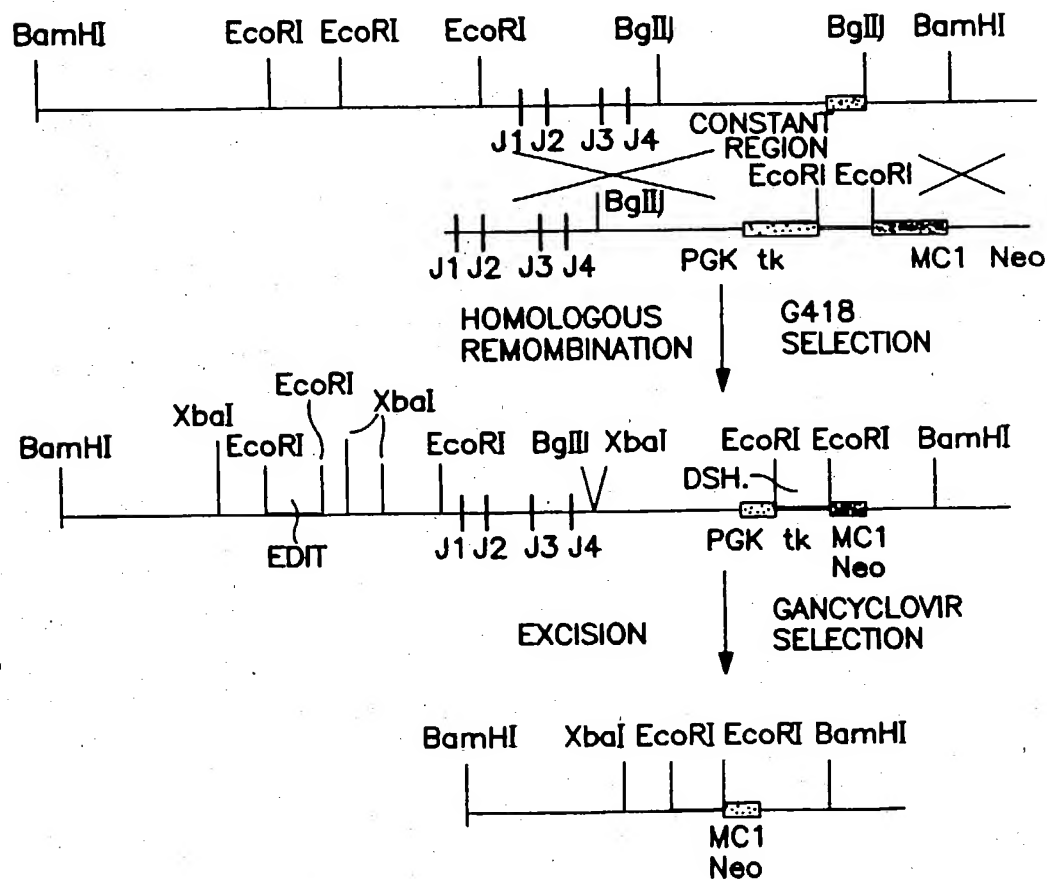


FIG. 8

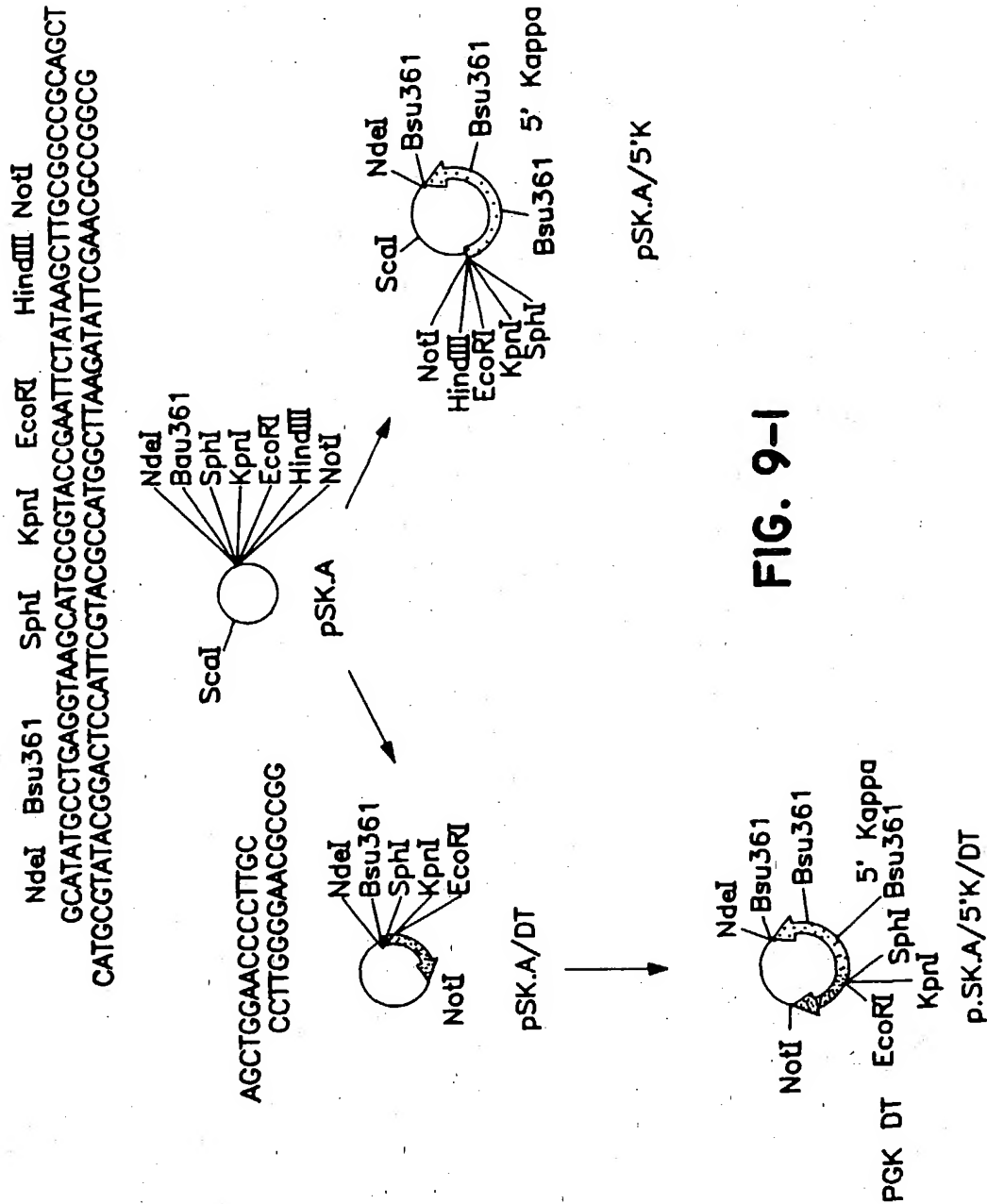


FIG. 9-I

SacI BamHI XhoI EcoRI HindIII NdeI
 GAGCTCGGATCCTATCTCGAGGAATTCTATAAGCTTCATATGTAGCT
 CATCCTCGAGCCTAGGATAGAGCTCCTTAAGATATTCAAGTATACA

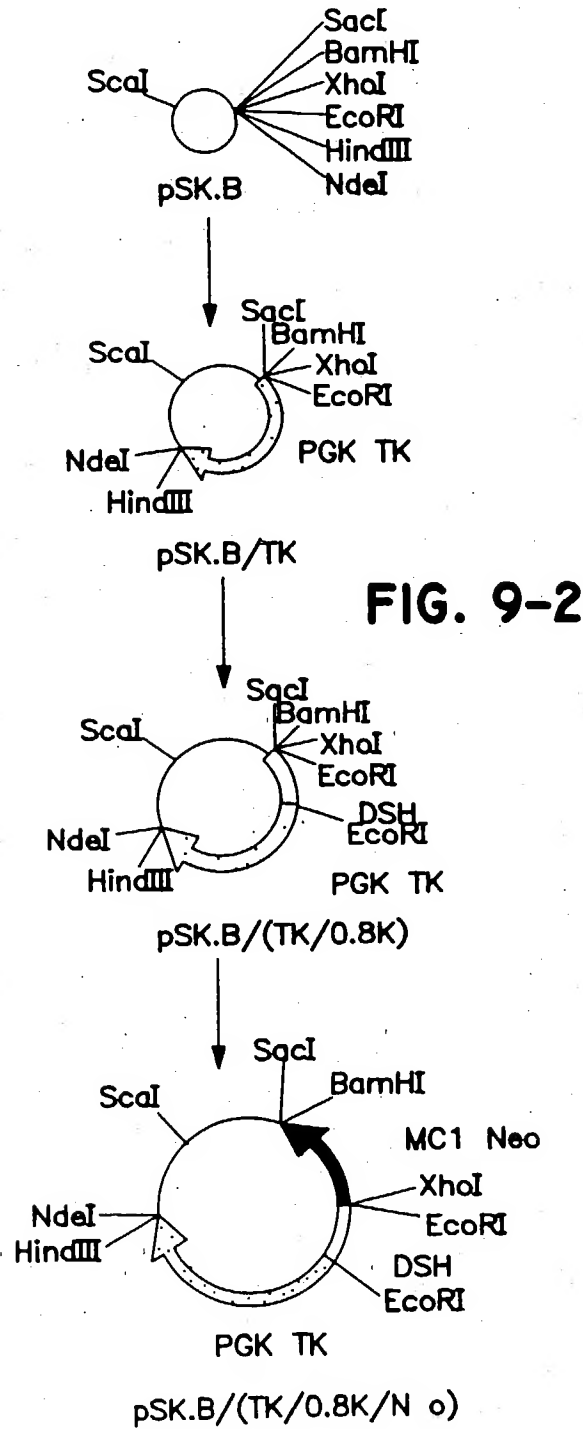


FIG. 9-2

HindIII EcoRI KpnI BamHI SacI NotI
 AAGCTTATAGAATTCGGTACCTGGATCCTGAGCTCATAGCGGCCGAGCT
 CATGTTTCAATATCTTAAGCCATGGACCTAGGACTCGAGTATCGCCGGCG

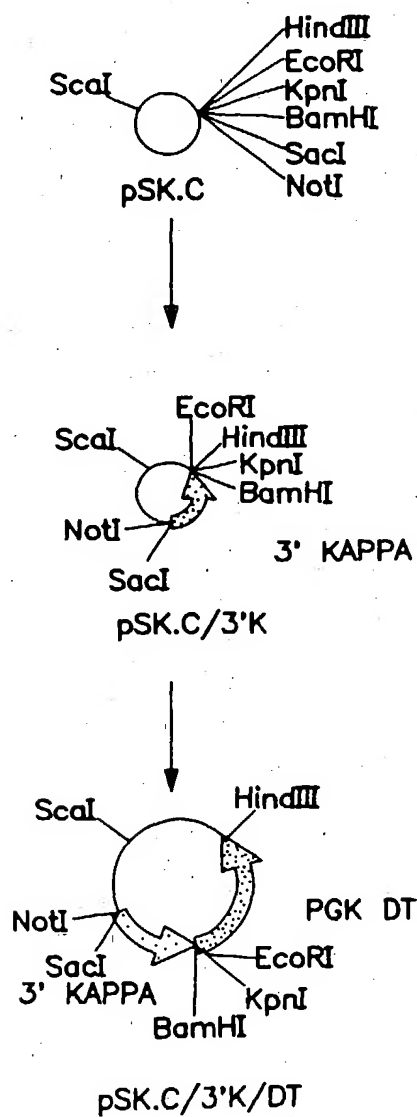
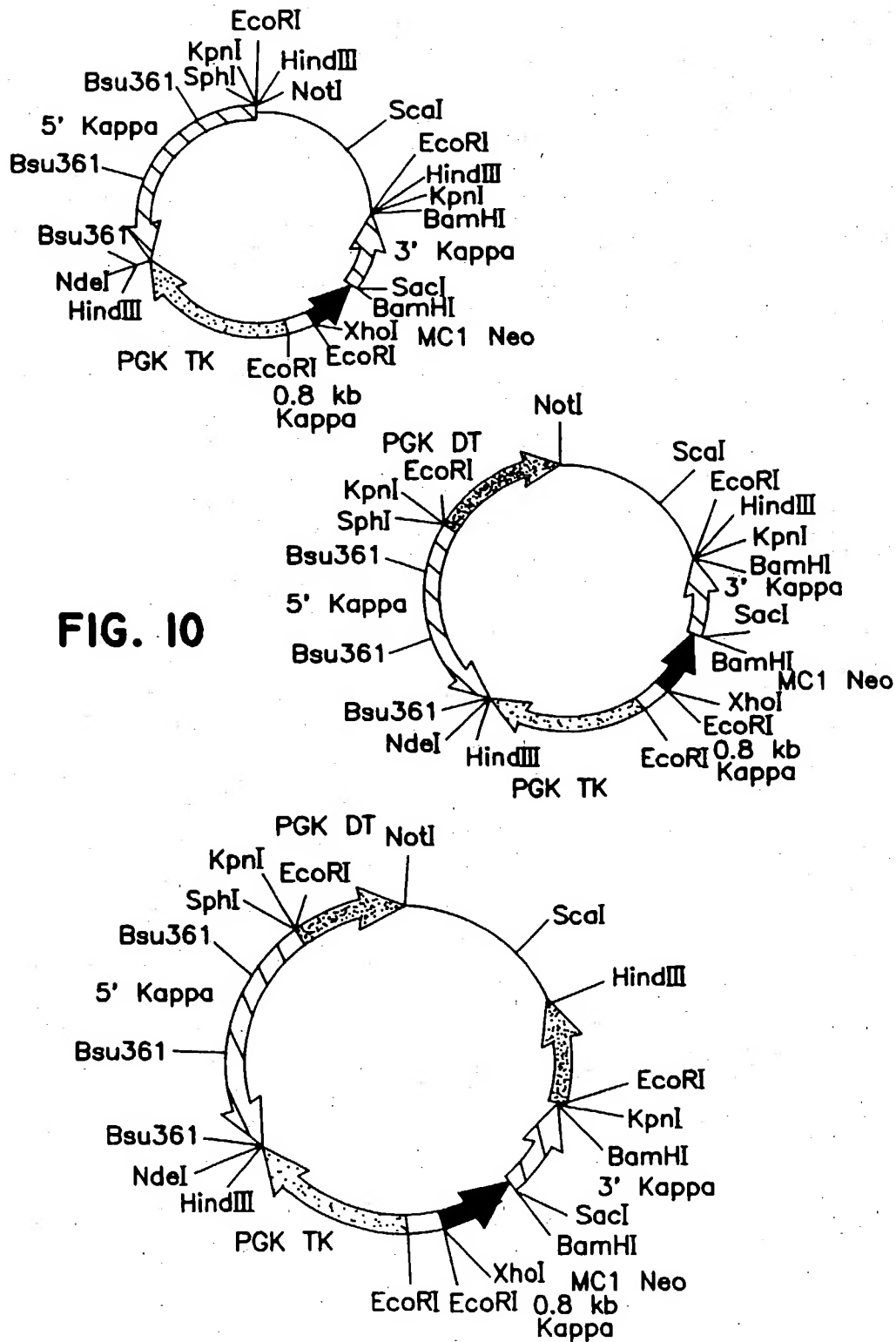


FIG. 9-3



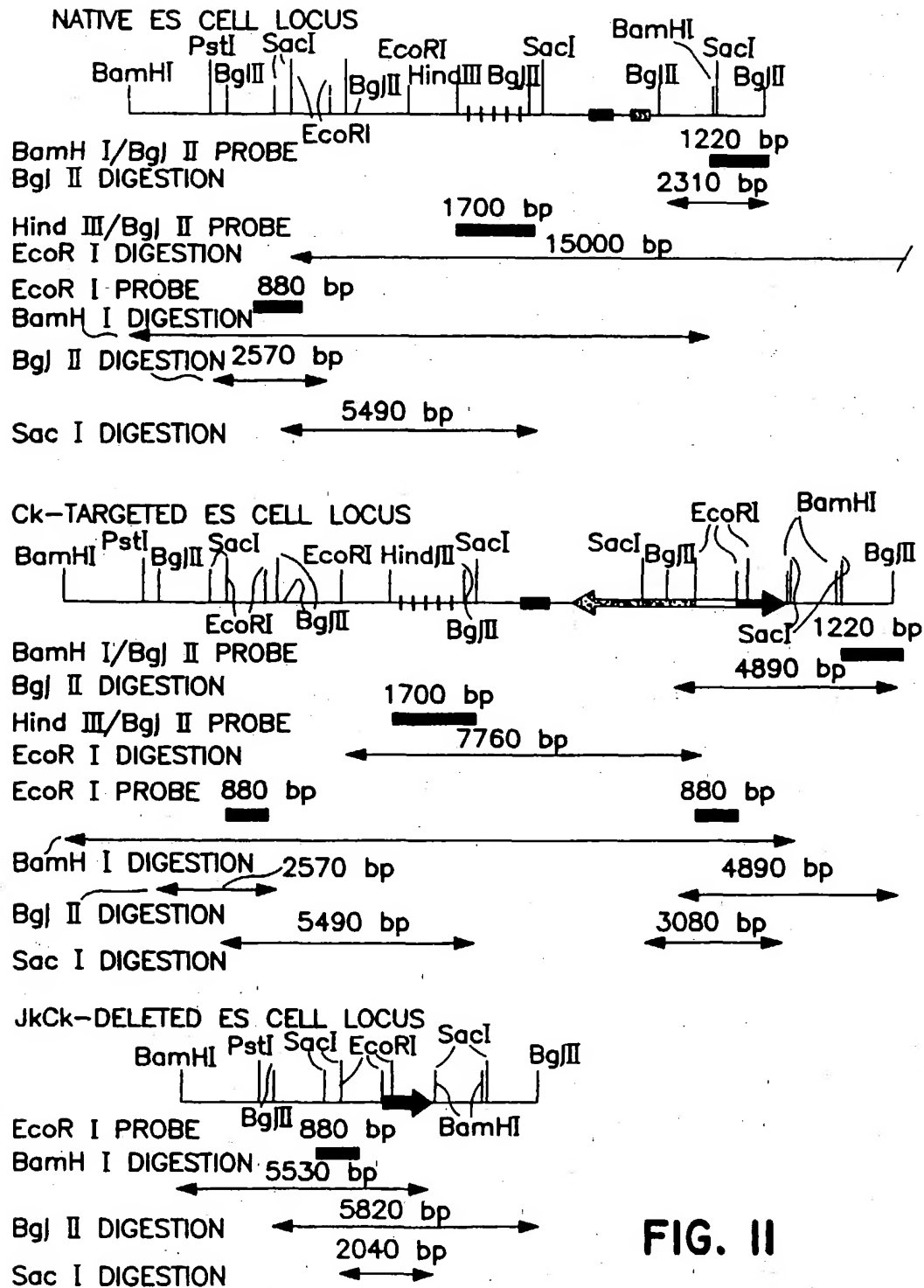


FIG. II

FIG. 12A

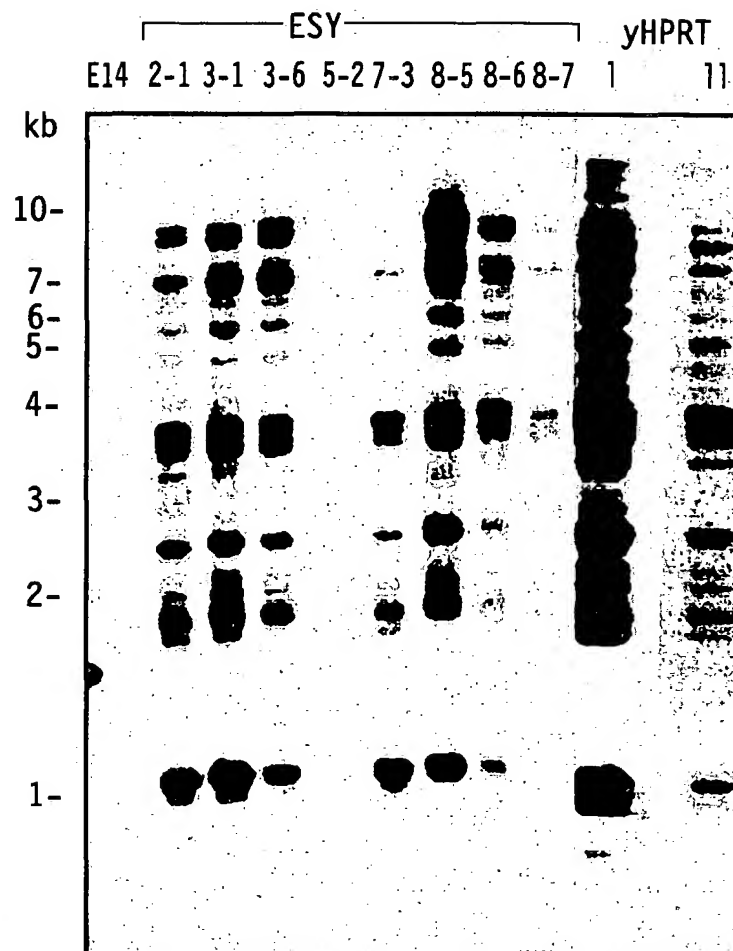


FIG. 12B

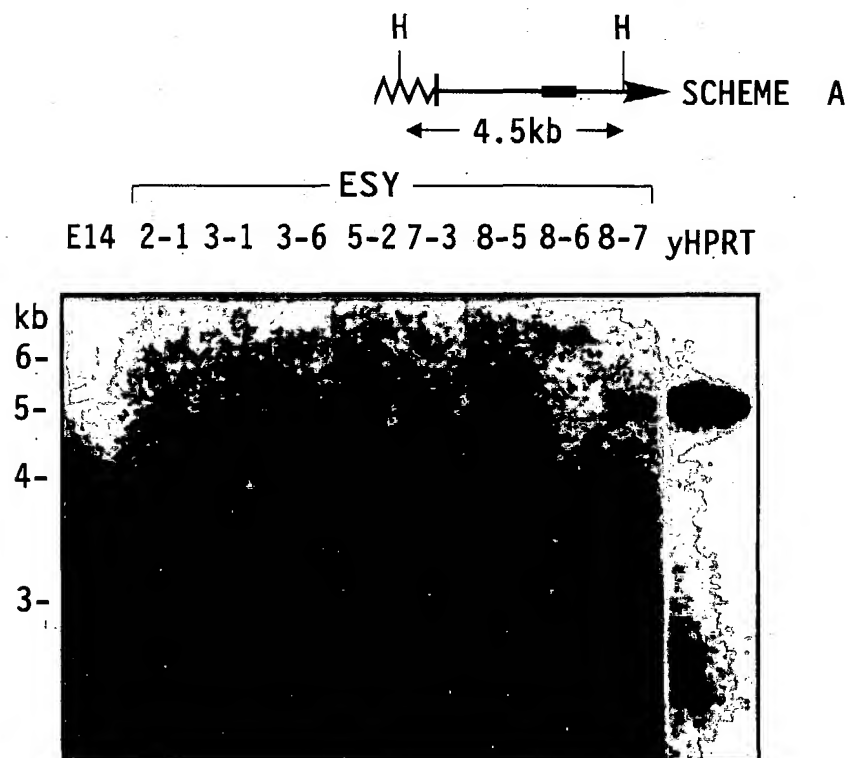


FIG. 12C

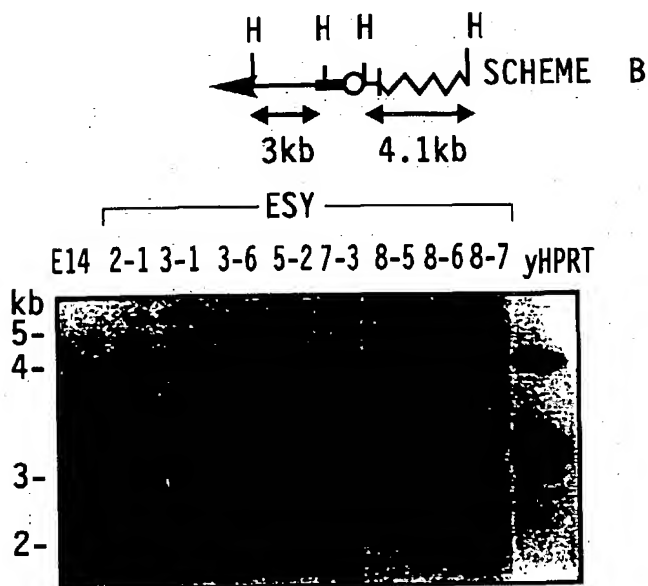


FIG. 12D

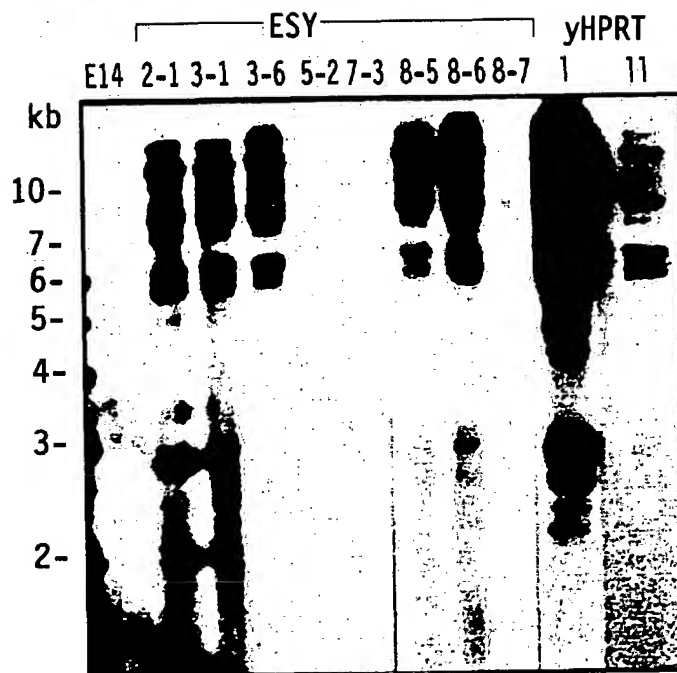


FIG. 12E

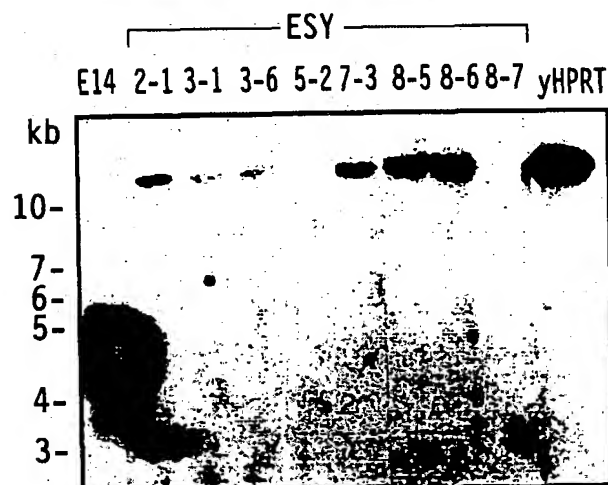


FIG. 13A

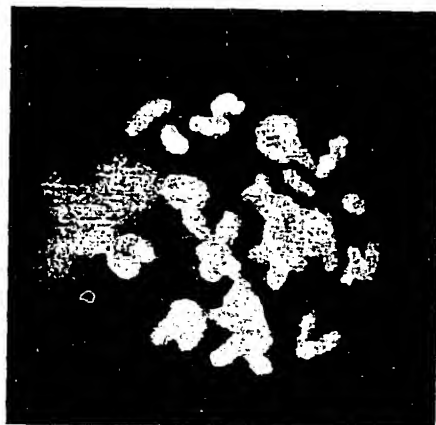


FIG. 13B

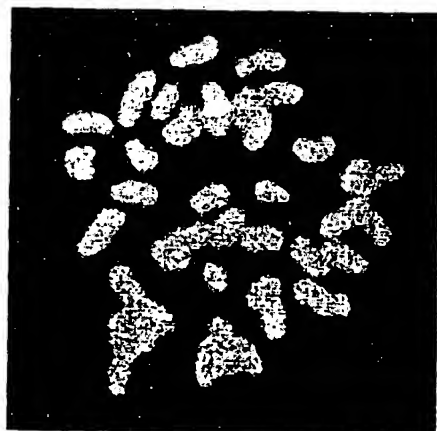
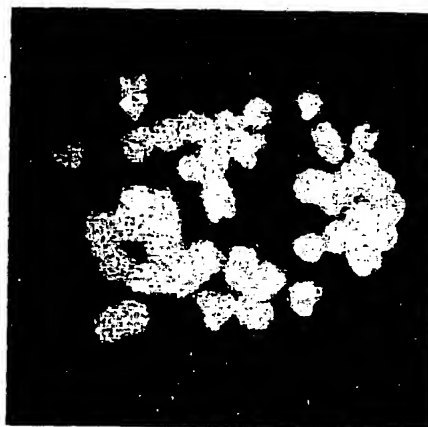


FIG. 13C

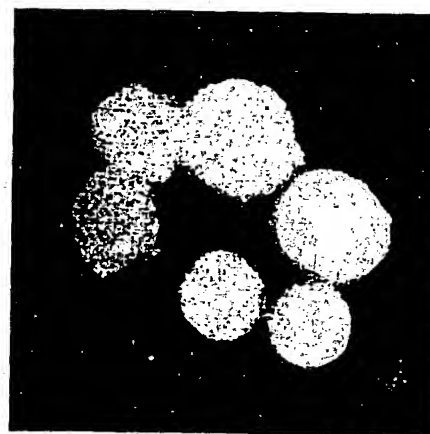


FIG. 13D

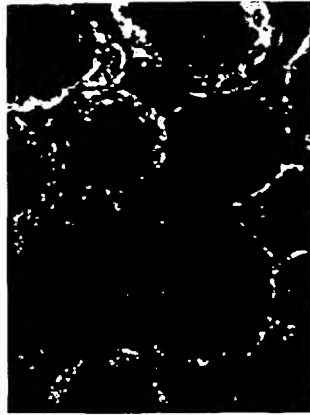


FIG. 14A



FIG. 14B



FIG. 14C



FIG. 14D

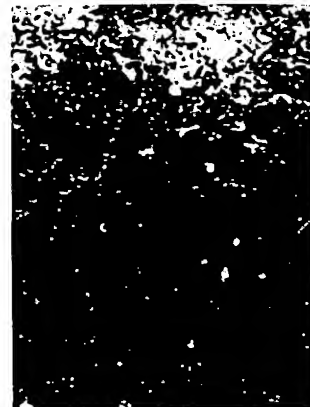


FIG. 14E



FIG. 14F

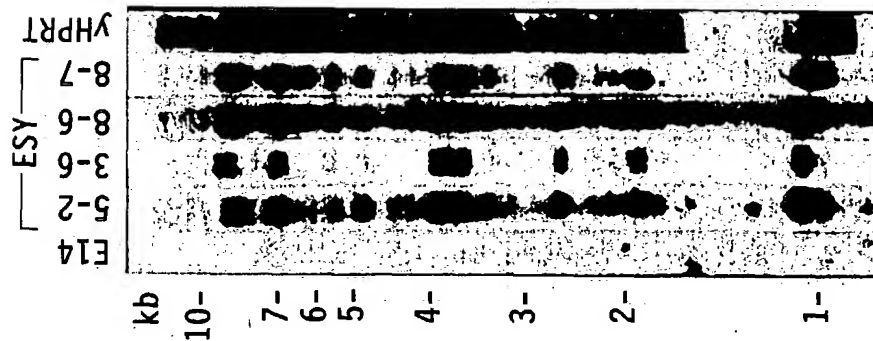
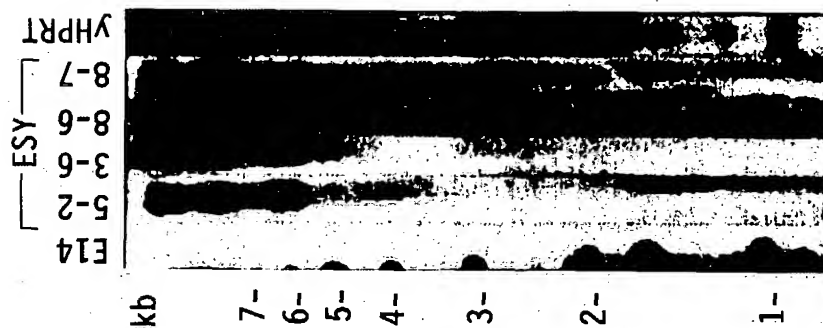


FIG. 14I

FIG. 14H

FIG. 14G

FIG. 14J

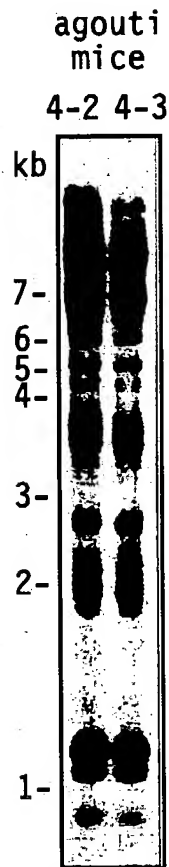


FIG. 14K

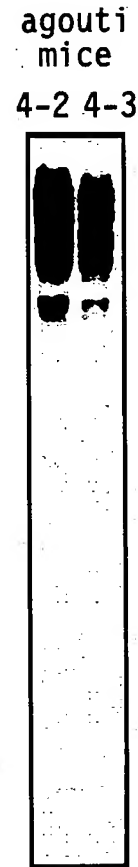


FIG. 15A

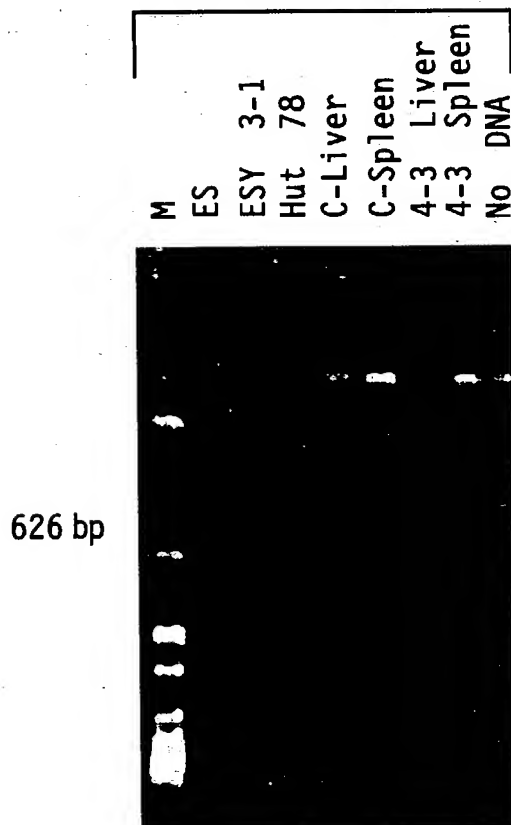
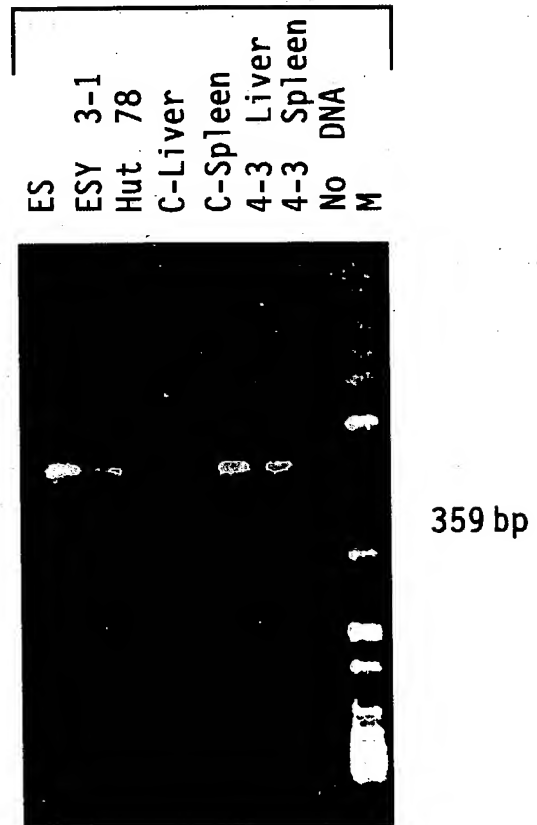
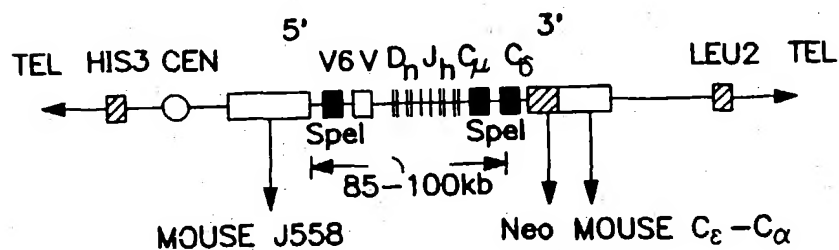
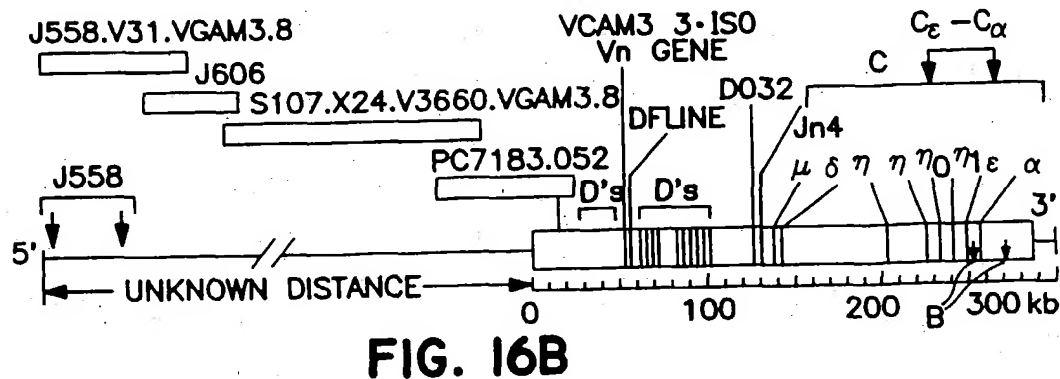
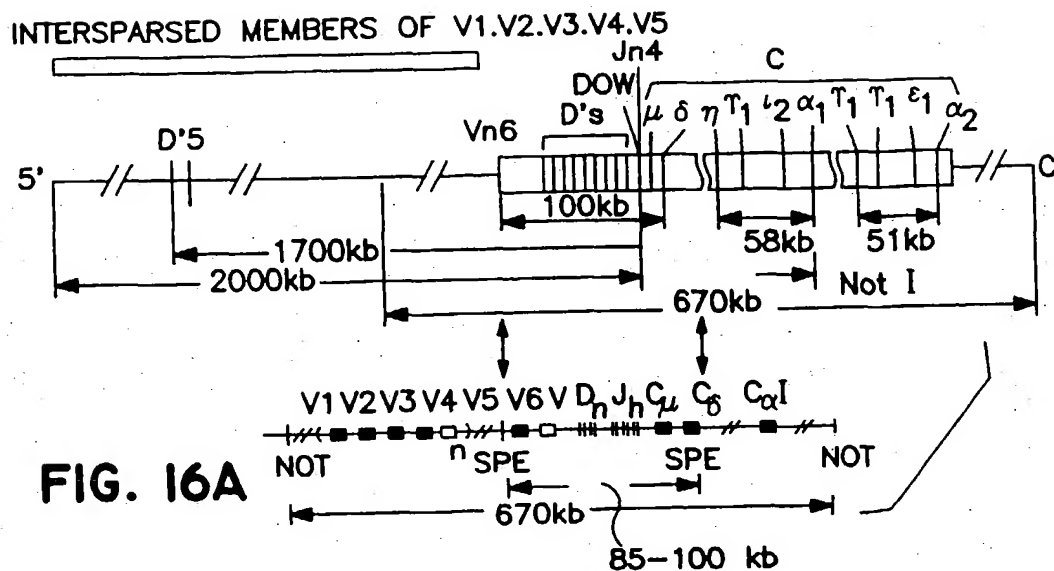


FIG. 15B





Mouse Breeding Scheme

Cross IA.

heterozygous inactive Murine IgH
 X
 heterozygous inactive Murine IgK

<u>MiGH (inactive)</u>	<u>MiGK</u>
<u>MiGH</u>	<u>MiGK</u>
X	
<u>MiGH</u>	<u>MiGK (inactive)</u>
	<u>MiGK</u>
↓	

F1 (cross I A)

<u>MiGH (inactive)</u>	<u>MiGK (inactive)</u>
<u>MiGH</u>	<u>MiGK</u>

Cross II.

F1 (cross I A) x F1 (cross I B)

F2 Quadruple Heterozygotes

<u>MiGH (inactive)</u>	<u>MiGK (inactive)</u>	<u>HiGH</u>	<u>HiGK</u>
<u>MiGH</u>	<u>MiGK</u>		

Cross III.

Intercross F2 mice

F3 DOUBLE Homozygotes

<u>MiGH (inactive)</u>	<u>MiGK (inactive)</u>	<u>HiGH</u>	<u>HiGK</u>
<u>MiGH (inactive)</u>	<u>MiGK (inactive)</u>		

FIG. 17

MAMMALIAN HOST GENOTYPES **FIG. 18A**

<u>Hetero- or Hemi-zygous Mice</u>	<u>Intercross Product Mice *</u>
I. $\frac{\Delta mlgL}{mlgL} \frac{mIgH}{mIgH}$	$\frac{\Delta mlgL}{\Delta mlgL} \frac{mIgH}{mIgH}$
II. $\frac{mIgL}{mIgL} \frac{\Delta mlgH}{\Delta mlgH}$	$\frac{mIgL}{mIgL} \frac{\Delta mlgH}{\Delta mlgH}$
III. $\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgH}{hIgH}$	$\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgH}{hIgH}$
IV. $\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgL}{hIgL}$	$\frac{mIgL}{mIgL} \frac{mIgH}{mIgH} \frac{hIgL}{hIgL}$
V. Animal I X Animal II	$\frac{\Delta mlgL}{\Delta mlgL} \frac{\Delta mlgH}{\Delta mlgH}$
VI. Animal III X Animal V	$\frac{\Delta mlgL}{\Delta mlgL} \frac{mIgH}{mIgH} \frac{hIgH}{hIgH}$ and $\frac{\Delta mlgL}{\Delta mlgL} \frac{\Delta mlgH}{\Delta mlgH} \frac{hIgH}{hIgH}$
VII. Animal IV X Animal V	$\frac{mIgL}{\Delta mlgL} \frac{mIgH}{\Delta mlgH} \frac{hIgL}{hIgL}$ and $\frac{\Delta mlgL}{\Delta mlgL} \frac{\Delta mlgH}{\Delta mlgH} \frac{hIgL}{hIgL}$
VIII. Animal VI X Animal VII	$\frac{\Delta mlgL}{\Delta mlgL} \frac{\Delta mlgH}{\Delta mlgH} \frac{hIgL}{hIgL} \frac{hIgH}{hIgH}$
	$\frac{mIgL}{\Delta mlgL} \frac{mIgH}{\Delta mlgH} \frac{hIgL}{hIgL} \frac{hIgH}{hIgH}$ and $\frac{\Delta mlgL}{\Delta mlgL} \frac{\Delta mlgH}{\Delta mlgH} \frac{hIgL}{hIgL} \frac{hIgH}{hIgH}$

*Not all possible genotypes from intercrosses are shown.

Δ	=	functionally inactive locus
m	=	mouse endogenous gene
h	=	human transgene
IgH	=	immunoglobulin heavy chain
IgL	=	immunoglobulin light chain

FIG. 18B